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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/448,867	11/24/99	BRINGHURST F	0609.4640001

HM12/0913
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EXAMINER	
WEGERT,S	
ART UNIT	**PAPER NUMBER**
1647	10

DATE MAILED: 09/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/448,867	Applicant(s) BRINGHURST ET AL.	
	Examiner Sandra Wegert	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *5-9 and 12-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 10-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-32* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement received 4/7/00 (Paper 5) has been entered into the record. Applicant's election of Invention I, without traverse, (claims 1-11) in Paper No. 10 is acknowledged. In addition, Applicant elected the following species: SEQ ID NO: 1. It should be noted that claims will be examined insofar as they read on the elected Invention and Species. Claims 5-9 and 12-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claim.

Claims 1-4 and 10-11 are under examination in the Instant Application.

Informalities

Specification

The disclosure is objected to because of the following informalities:

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is *suggested*: "MODIFIED HUMAN PARATHYROID HORMONE".

Appropriate correction of the title is required.

Abstract

The abstract of the disclosure is objected to because it is not in narrative form. See MPEP § 608.01(b).

Appropriate correction is required.

Sequence Rules

The instant application is not fully in compliance with the sequence rules, 37 CFR 1.821-1.825, especially 1.821, part (c), because each disclosure of a sequence embraced by the definitions set forth in the rules must be accompanied by the required reference to a unique sequence identifier (i.e., SEQ ID NO:). This occurs in Figs. 1-4, for example. Sequence identifiers for a Figure may be placed in the Figure itself or in the Brief Description of the Drawings corresponding to that figure.

Appropriate correction is required.

Claim Rejections/Objections

35 *USC § 101, - non-statutory*

35 U.S.C. 101 reads as follows:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.**

Claims 1-4 and 10-11 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1 and 2 and dependent claims read on a product of nature in that

the claimed polypeptide is not isolated or modified. Amending the claims to read "isolated" or "purified", etc. would be remedial.

35 USC § 112, first paragraph - scope

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> ***The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.***

Claims 1-4 and 10-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the peptide comprising SEQ ID NO: 1, does not reasonably provide enablement for all variants of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are directed to parathyroid hormone analogues. The specification discloses a PTH polypeptide having an amino acid sequence shown in SEQ ID NO: 1, as well as methods for using specifically modified fragments of the PTH polypeptide. The scope of the patent protection sought by the Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons:

The specification discloses an enabled utility for PTH (1-34) and PTH (1-28), when the first amino acid is desamino-Ala or desamino-Gly, to be used as agonists at the PTH receptor. The instant case claims altering as much as 10% of the polypeptide claimed in SEQ ID NO: 1. However, the art shows that peptide families have members with high structural similarities but disparate functions. For example, Smith et al. (1997, Nature Biotechnology 15:1222-1223) demonstrate that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of

function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. The possible effect of changing even one amino acid in a polypeptide can be seen in Wells (1990) in which certain single amino acid substitutions in various positions of subtilisin dramatically altered its binding characteristics, while mutations of other residues had no effect. Finally, Kopchick, et al (1994, US Patent 5,350,836) showed that small modifications at a single residue changed Bovine Growth Hormone from an agonist to an antagonist. This reference and others demonstrate that it is not predictable as to which amino acids are necessary to maintain the functional characteristics of a protein.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Due to the large quantity of experimentation required to determine how to use all variants of SEQ ID NO: 1, the lack of direction or guidance in the specification regarding same - e.g., the lack of guidance regarding specific activity of SEQ ID NO: 1 with the first and nineteenth amino acid unspecified, or at least 90% identical-, the lack of working examples to all variants of SEQ ID NO: 1, the state of the art showing the unpredictability of function based on structural similarity of hormone polypeptides, and the breadth of the claims which embrace innumerable variants of SEQ ID NO: 1, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being unpatentable over Lewis, et al, 1993 (UK Application GB 2,269,176-A). Lewis et al. disclose a polypeptide sequence which is 98.5% identical to SEQ ID NO: 1 in the instant application. This reference meets the limitations of claim 1 and dependent claims of "at least 90% identity" and "consisting essentially of" the amino acid sequence of SEQ ID NO: 1.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being unpatentable over Willick, et al, 1996 (US Patent 5,556,940). Willick et al. claim a polypeptide sequence which is 97.8% identical to SEQ ID NO: 1 in the instant application. This reference meets the limitations of claim 1 and dependent claims of "at least 90% identity" and "consisting essentially of" the amino acid sequence of SEQ ID NO: 1.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being unpatentable over Chu, et al, 1975 (Biochem 14:3631). The paper of Chu et al. discloses a polypeptide sequence that is 97.8% identical to SEQ ID NO: 1 in the instant application. This reference meets the limitations of claim 1 and dependent claims of "at least 90% identity" and "consisting essentially of" the amino acid sequence of SEQ ID NO: 1.

Conclusion: Claims 1-4 and 10-11 are not allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW

8/31/01

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER